

METHOD OF TREATING INFLAMMATION IN THE JOINTS OF A BODY

BACKGROUND OF THE INVENTION

Claim of Priority

The present application is a divisional patent application of previously filed application having Serial No. 09/778,397 filed on February 2, 2001 which is set to mature on November 11, 2003 as U.S. Patent Number 6,645,485 which claims priority to U.S. provisional patent application having Serial No. 60/202,561 filed on May 10, 2000 and U.S. provisional patent application having Serial No. 60/214,592 filed on June 27, 2000 also incorporated herein by reference.

Field of the Invention

The present invention relates to a process of treating inflammation in a joint, such as but not limited to a knee joint, a hip joint or an ankle joint, which has been damaged or which has otherwise become defective, and thereby, alleviating pain, heat, redness, swelling, stiffness, and other difficulties typically associated with a damaged or defective articular cartilage surface in a joint. More in particular, the present invention is directed to a process of injecting a mixture of purified growth hormone (commonly known as somatotropin) and a buffer solution into the joint of a body, preferably but not limited to that of a human, so as to initiate the treatment

1 process.

2
3 DESCRIPTION OF THE RELATED ART

4 The ends of bones which form a joint, including vertebra,
5 are covered by articular cartilage, which is a thin, fragile
6 tissue layer and which allows the bone ends to move freely and
7 without pain. Many arthritic diseases and many degrees of
8 trauma can, however, cause destruction or deterioration of this
9 fragile layer. From ancient times and continuing in the present
10 day, people have suffered through varying degrees of heat,
11 redness, pain, swelling and/or stiffness of the joints, any one
12 or all of which can often be associated with deterioration of
13 the articular cartilage in the joints, whether those joints are
14 associated with walking, such as the hip, knee or ankle joints
15 or others, such as the vertebra of the spine, the shoulder,
16 elbow or wrist joints and fingers. Regardless, damage to and/or
17 the deterioration of articular cartilage in a joint is often, if
18 not always accompanied by inflammation. Inflammation, which is
19 typically thought of as heat, redness, pain, swelling and/or
20 stiffness, when experienced in a joint, can be crippling.

21 As a result, many have tried to develop ways to alleviate
22 the pain and inflammation associated with arthritis and other
23 damage to the joints. A number of these efforts have focused on
24 oral medications such as cortisone derivatives (steroids) and
25 numerous non-steroidal anti-inflammatory drugs (NSAIDs), all of

1 which have potentially serious side effects. Other efforts have
2 focused on implants of entire joints, such as the knee or hip,
3 although typically, a lengthy and complicated surgical procedure
4 is required, with the patient being forced to undergo a
5 significant recovery period, including a rigorous and costly
6 regimen of physical therapy thereafter. Most often, full motion
7 and full activity are not achieved with the use of these
8 implants. While medical science has recently developed a
9 variety of new materials for the joint implants, these implants
10 are often more costly, offer results which may be only
11 marginally better than those obtained previously, and do nothing
12 to avoid the hospitalization required for the surgical
13 implantation of them nor the long periods of rehabilitation. In
14 addition, it is also possible that one or more revision
15 surgeries will be needed to replace defective, loose or infected
16 implants. Further, the general discomfort which might be
17 associated with utilizing such implants makes an alternative
18 method all the more desirable.

19 The biological action of growth hormone, namely,
20 somatotropin, has been the subject of the inventor's research.
21 Heretofore, growth hormone has been used clinically to enhance
22 the growth of children with short stature. Somatotropin may
23 have other effects on other organ systems but in the instant
24 application for a patent, the specific actions of somatotropin
25 related to its effects on articular cartilage have been focused

1 on by Dunn's research and are utilized herein. The major
2 targets of somatotropin activity are believed by the inventor
3 hereof to be vascular sinusoids and sub-chondral vessels located
4 at the cartilage-bone interface (sub-chondral bone) and the
5 endothelial cells located therein, and in addition, nests of
6 stem (pleuripotential) cells in various sites such as marrow;
7 and the vascular system. More specifically, it is believed by
8 the inventor hereof that growth hormone has the ability to
9 stimulate proliferation of stem cells in the marrow and
10 subchondral vessels and sinusoids. The inventor hereof has also
11 shown that growth hormone has the ability to form vascular and
12 multi-lumen sinusoids, known as Glomeruloids, from pre-existing
13 and mature single lumen vessels in the sub-chondral bone. The
14 inventor describes this action of growth hormone as Morphogenic
15 Action, which is a type of rejuvenation of mature monolumen
16 vessels into fetal-like and/or other immature chondrogenic
17 vascular structures. This Morphogenic Action, a type of
18 rejuvenation, can also dematurate a layer of mature sub-chondral
19 bone into a cartilaginous state comparable to that observed in
20 the neonatal and immature cartilaginous skeleton.

21 The method of this invention relies on a novel use of
22 growth hormone, namely, somatotropin. More in particular, the
23 method of the present invention is useful as an anti-
24 inflammatory agent and is specifically adapted to treat
25 inflammation (heat, redness, pain, swelling, stiffness, etc.)

1 and/or pain associated with damaged and/or defective articular
2 cartilage on or at a joint in a body through the injection
3 directly into the joint of one or more dosages of purified
4 growth hormone (somatotropin). There is no reliance on the
5 transplantation of tissue and thus all of the detrimental
6 conditions of rejection, immune reaction, and other causes of
7 transplant failure are avoided. Similarly, the present
8 invention does not require an individual to undergo a lengthy or
9 complicated surgical procedure, such as those which accompany
10 joint replacements.

11 Until the present invention, growth hormone has not, to the
12 inventor's knowledge, ever been used to treat merely the
13 inflammation of tissues such as the soft tissue components
14 within and surrounding a joint, i.e., synovial lining, capsule,
15 and ligaments and articular cartilage and/or the pain associated
16 therewith. Of course, the inventor herein has heretofore
17 focused on growth hormone as a means for regenerating articular
18 cartilage in a joint, for which U.S. Patent No. 5,368,051 was
19 awarded, incorporated herein by reference, but he has since
20 improved and refined the applications for which growth hormone
21 may be used, as set forth in greater detail, below.

22 Accordingly, the method of the present invention provides
23 a much needed improvement in the treatment and elimination of
24 ailments associated with the deterioration or destruction of the
25 articular cartilage surface of a joint, including pain,

1 inflammation of the soft tissue components within and
2 surrounding the joint, including heat, redness, pain, swelling
3 or stiffness. The method of the present invention also is
4 directed towards providing for the reappearance or increase of
5 space between bone ends and restoration of normal alignment of
6 a limb, such as a leg, and including the restoration of normal
7 or nearly normal motion.

8 9 SUMMARY OF THE INVENTION

10 The present invention is directed towards a method of
11 treating inflammation and pain in a joint separating two or more
12 bones. It is pointed out that for purposes of this application,
13 inflammation means pain, joint stiffness, redness, heat and/or
14 swelling, etc.

15 The method comprises an initial step of dissolving a
16 quantity of growth hormone in a buffer solution and then
17 injecting the resulting mixture as a single loading dose into
18 the joint cavity where it will lessen the inflammation of the
19 synovial lining, joint capsule, ligaments and articular
20 cartilage. If desired or needed, additional injections of
21 growth hormone of a single dosage can be injected from one day
22 to several weeks later and after a first set of single or
23 multiple injections, several additional sets of single or
24 multiple injections may be given so as to maintain any
25 improvement of the function of the joint.

1 In one alternative embodiment, the method of the present
2 invention may comprise an additional step of mixing an amount of
3 Lidocaine, anywhere from about 0.5 milliliter to 10 milliliters,
4 and ideally about 1 to 3 milliliters of Lidocaine with the
5 mixture of growth hormone and buffer solution. It is
6 contemplated that other injectable anesthetics aside from
7 Lidocaine might also be used with the present invention.

8 It is a primary object of the present invention to provide
9 a method for reducing the inflammation of tissue located in or
10 at the joints of a body as well as pain arising at or within the
11 joint of a body without requiring a surgical procedure.

12 It is also a primary object of the present invention to
13 provide a new treatment for pain and inflammation in the joint
14 of a body which relies upon a lower dosage of growth hormone and
15 an alternative buffer solution other than that described
16 previously in the applicant's U.S. Patent No. 5,368,051 directed
17 to regenerating articular cartilage.

18 A feature thought to arise following treatment of a joint
19 with the present invention is that contact or near contact
20 between the bone-to-bone surfaces is reversed, meaning that a
21 separation, distance or space between the bony surfaces is
22 restored, presumably but perhaps not exclusively because the
23 treatment causes some resumption of growth of articular
24 cartilage, such as that which has been worn down.

25 An advantage of the present invention over that disclosed

1 in the Applicant's previous patent is that a range of motion is
2 restored to a joint following treatment.

3 Another advantage of the present inventive treatment is the
4 smoothing of irregular joint surfaces and sub-chondral bone and
5 also a reversal of malalignment of the limb following treatment.
6 The present invention thereby eliminates or substantially
7 alleviates ailments in the joints.

8 These and other objects, features and advantages of the
9 present invention will become more clear when the drawings as
10 well as the detailed description are taken into consideration.

11 12 BRIEF DESCRIPTION OF THE DRAWINGS

13 For a fuller understanding of the nature of the present
14 invention, reference should be made to the following detailed
15 description taken in connection with the accompanying drawings
16 in which:

17 Figure 1 is a cross-sectional view of a joint surface
18 illustrating a deteriorated articular cartilage on the lower
19 joint surface.

20 Figure 2 is an isolated view illustrating the injection of
21 a growth hormone and buffer solution in the joint cavity.

22 Like reference numerals refer to like parts throughout the
23 several views of the drawings.

24 25 DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

1 The present invention is directed specifically towards a
2 method of treating inflammation and associated pain in a joint,
3 such as one having damaged or defective articular cartilage 10.
4 Articular cartilage 10, which is present between bones 15 at a
5 joint 20, provides a bearing type surface for facilitated
6 movement between the bones 15. If articular cartilage is
7 damaged or deteriorated, as represented by reference numeral 30
8 in the drawings, this can result in a person's experiencing
9 significant heat, redness, pain, swelling, stiffness and/or
10 malalignment of the limb or joint, and can even be crippling to
11 some individuals, such as those suffering from a trauma or other
12 ailments which destroy the joint surface. The articular
13 cartilage 10 is a resilient layer of tissue which covers the
14 ends of bones 15, and it has been traditionally assumed that
15 once gone, it cannot be regrown or regenerated, at least until
16 the work by the inventor hereof, some of which has been set
17 forth in U.S. Pat. No. 5,368,051.

18 The method of the present invention is a significant
19 improvement over what is known in the art for treating the
20 sometimes excruciating pain which individuals experience in one
21 or more of the joints of their bodies. For example, the present
22 invention does not involve a surgical procedure, which would
23 require some recovery therefrom, nor any type of transplantation
24 of tissue. The method of the present invention, which is
25 believed to offer swift relief to the heat, redness, pain,

1 swelling, stiffness or other inflammatory symptoms experienced
2 by individuals suffering from damaged articular cartilage in a
3 joint, offers an improvement over the method described in the
4 inventor's previous U.S. Pat. No. 5,368,051 by relying upon the
5 utilization of a lower dosage of growth hormone and of an
6 alternative buffer solution, and if desired, the addition of
7 injectable anesthetics. The method of the present invention is
8 thought to be effective as a result of the discovery that in
9 addition to the metaphyseal growth plate which exists near the
10 ends of bones and which makes the bones grow during the immature
11 and adolescent periods, there is also an articular growth plate
12 at the joint surface. The metaphyseal growth plate, once
13 achieving full growth within the bone, ceases to function in an
14 adult and disappears. The articular growth plate, however,
15 remains intact, although growth-inactive, at the joint surface
16 in the adult. When properly stimulated by injecting purified
17 growth hormones in the joint, including an anesthetic if
18 desired, as in the method(s) of the present invention, there
19 would be no need for surgically exposing the joint, nor for
20 debriding it; the pain and inflammation associated with the
21 damaged articular cartilage is relieved, and this is thought to
22 be because the articular growth plate is stimulated so as to
23 resume active growth.

24 With reference now to Figure 1, when an articular cartilage
25 defect as at 30 is present in the joint of an individual,

1 whether a hip joint, knee joint, ankle joint or other type of
2 joint, such that it causes him or her sufficient pain to seek
3 out medical treatment, it is preferable that the individual be
4 required to undergo certain tests in an effort to determine
5 whether treatment in accordance with the present invention is
6 advisable. For example, it is preferred that the individual
7 undergo a complete physical examination by a licensed physician,
8 including any X-rays, MRIs, and/or other laboratory work that
9 may be recommended to hopefully rule out the presence of
10 serious, acute or chronic illnesses and/or whether the
11 individual has a pre-existing excess amount of growth hormone.
12 That is because it is preferred that such persons would not be
13 treated in accordance with the present invention.

14 Turning more specifically to the method of the present
15 invention, it is directed preferably for use on humans; however,
16 it can be similarly effective with other animals so long as the
17 necessary growth hormone, preferably purified growth hormone, is
18 utilized. It is preferred that the growth hormone be species
19 specific which means that human growth hormone would be used on
20 humans; cattle (bovine) growth hormone would be used on cattle;
21 and horse growth hormone would be used on horses, etc. More in
22 particular, it is preferred that the growth hormone (known as
23 somatotropin) utilized be identical to naturally produced growth
24 hormones of that species. If a biologically engineered hormone
25 alternative were to be used, it should have an amino acid

1 sequence identical to the natural hormone. In the most
2 preferred embodiments, the growth hormone is biologically
3 engineered to exactly duplicate the natural hormone and to
4 assure maximum purity, and avoid the possibility of transmitting
5 disease. For example, if the growth hormone is to be prepared
6 from pituitary glands retrieved from cadavers, the hormone
7 preparation may transmit rare forms of neurological disease even
8 though it may be highly purified.

9 More in particular, the method of the present invention
10 generally comprises the steps of dissolving a quantity of growth
11 hormone, preferably somatotropin that has ideally been
12 biologically engineered so as to be in a purified state, in a
13 buffer solution and then injecting the resulting solution into
14 the joint having damage which causes an individual to experience
15 pain or inflammation. The quantity of growth hormone to be
16 dissolved in the buffer solution is discussed in greater detail
17 below. The purified growth hormone is typically in the form of
18 a powder and as such, may be readily dissolved in a buffer
19 solution. Preferably, the buffer solution has a range of pH
20 between 5.5 and 8.3, although more preferably, the range of pH
21 is between 6.0 and 8.0. Generally, buffer solutions include a
22 saline solution and have a pH range of approximately 7.0 to 7.4
23 which is the range of biological pH. In a preferred embodiment,
24 the buffer solution comprises a phosphate buffer which may also
25 include a preservative. In an alternative embodiment, the

1 buffer solution is Hank's Buffer Solution having a higher pH
2 range of about 8.0. Other preparations of purified growth
3 hormone may, due to their chemical composition, require buffer
4 solutions of other ranges of pH.

5 The growth hormone to be dissolved in the buffer solution
6 can be in a range of between 0.5 milligrams and 10.0 milligrams
7 of growth hormone per milliliter of buffer solution, although a
8 most preferred dosage of about 5.0 to 7.0 milligrams growth
9 hormone, and ideally, 5.8 milligrams of growth hormone per
10 milliliter of buffer solution would be used. This dosage is
11 thought to be operative in accordance with the present inventive
12 method for most human individuals. An alternative dosage to be
13 administered can be more closely related to the person's and/or
14 animal's weight, and will be in the preferred range of 0.025
15 milligrams to 0.249 milligrams per Kilogram of body weight.

16 Once the growth hormone and buffer solution have been
17 mixed, a single dosage of the mixture is injected to the joint,
18 as illustrated in Figure 2. The growth hormone is injected,
19 such as by utilizing a syringe 70, into the joint space and not
20 directly into the bone 15 or tissue. In this manner, it may
21 flow over the entire joint surface and react initially with the
22 tissues on the surface and then with all the vascular units 40
23 at the bone-cartilage interface. A portion of the purified
24 growth hormone may be absorbed into the bloodstream after about
25 four hours. One of the systemic effects associated with this

absorption into the general circulation will be to stimulate production of stem cells in the marrow, vascular system and other areas outside the joint. The growth hormone will cause a reaction in the subchondral vascular structures so as to promote local production of endothelial derived stem cells and also to attract pluripotent cells to the sinusoidal layer of the bone, the pluripotent cells being collected in these vascular structures. The reaction will initiate cell layer growth at the sub-chondral layer, and it is believed will eventually produce enough cartilage to form additional joint surface and lead to there being an increased space between the bones of the joint being treated in accordance with the present invention. Depending on the individual patient's condition, repeated, periodical injections of the growth hormone may be required. For example, another single dosage may be injected into the joint in about four weeks, and repeated in another four weeks. Injections could be given and repeated at other time intervals, however, such as every two weeks. Alternatively, single or multiple injections can be given one day, several days, to several weeks or months apart. Such repeated injections of somatotropin or growth hormone may be necessary in situations where a patient suffers from a disease which will continuously impair or destroy the cartilage surface, or antagonize the action of the growth hormone. It is further contemplated that the injection of growth hormone according to

1 the present invention could include the addition of chemical
2 substances which will block or impede the antagonistic action of
3 proteases, present in certain diseases, that might impair or
4 prevent the beneficial action of the growth hormone within the
5 joint.

6 In an alternative embodiment, the method of the present
7 invention may comprise an additional step of mixing Lidocaine or
8 another local anesthetic with the mixture of growth hormone and
9 buffer solution prior to injection into the joint. In this
10 embodiment, the amount of Lidocaine or other anesthetic to be
11 mixed with the growth hormone and buffer solution may be
12 anywhere from 0.5 milliliters to 10 milliliters, although
13 preferably, about 1 to 3 milliliters will be used.

14 From the preceding, it is recognized that the present
15 invention may also be considered to include a beneficial anti-
16 inflammatory composition and/or an analgesic composition, both
17 of which may, of course, be utilized within the previously
18 defined methods. Specifically, the anti-inflammatory and/or
19 analgesic composition may comprise a purified growth hormone of
20 between 0.025 milligrams to 0.249 milligrams per kilo of a
21 patient's body weight dissolved in a buffer solution of
22 approximately between 1 to 10 milliliters, preferably as
23 described with regard to the method of treatment, or a purified
24 growth hormone of approximately between 0.5 milligrams to 10.0
25 milligrams per milliliter of the buffer solution, also

1 preferably as previously recited. Further, a local anesthetic
2 agent, anti-protease agent and/or anti-enzyme agent may be
3 included therewith. In the case of the local anesthetic, it may
4 preferably include Lidocain in an amount of generally between
5 about 0.5 milliliter to 10 milliliters.

6 Since many modifications, variations and changes in detail
7 can be made to the described preferred embodiment of the
8 invention, it is intended that all matters in the foregoing
9 description and shown in the accompanying drawings be
10 interpreted as illustrative and not in a limiting sense. As
11 examples, the present invention is also claimed in terms of a
12 method for increasing a patient's range of motion in a joint as
13 well as reducing the mal-alignment of a patient's arthritic
14 joint, the latter of which can be characterized as a bow-legged
15 deformity when the joint involved is the knee. In other words,
16 it is the inventor's belief that the intra-articular
17 injection(s) of growth hormone into joint(s) restores normal
18 alignment of osteo-arthritic and post traumatic arthritic knees,
19 such that a bow leg deformity may disappear and the leg can
20 regain normal alignment, and further, or alternatively, that it
21 can restore normal or nearly normal motion in both extension and
22 flexion in osteo-arthritic and post traumatic arthritic knees or
23 other joints. This increased range of motion can be assisted by
24 therapeutic exercise(s), which normally, without treatment in
25 accordance with the present invention, would be extremely

1 painful. In many cases then, therapeutic exercises can only be
2 carried out following treatment with the present invention in as
3 much as the present invention reduces the pain experienced by
4 the patient so as to permit the exercise(s) to occur at all. As
5 another example, the inventor believes that the method of the
6 present invention can be used to treat and/or increase the joint
7 spaces between the vertebrae of the spine, as well. Thus, the
8 scope of the invention should be determined by the appended
9 claims and their legal equivalents.

10 Now that the invention has been described,